REMARKS

The claims have been amended to make it explicit that what is being claimed is treatment of side effects oh hemodialysis in patients undergoing hemodialysis.

To the extent that they remain relevant, applicants reaffirm the statements made in the response of March 31 to the final rejection of December 3, 2008.

In the interview of June 3, the fact that the present invention was directed to treatment of oxidative stress and not to treatment of diabetes as such was discussed but no conclusion was reached as to an allowable form of claim. During the discussion, it was suggested that incorporation into the etiology of the oxidative stress into the claim might help. This has now been done by stating thet the oxidative stress is the result of the hemodialysis.

> In the advisory action, the examiner formulates the obviousness argument as follows: In view of the combined teachings of the prior art, one skilled in the art would have been motivated to administer cysteine to treat oxidative stress resulting from hemodialysis with a reasonable expectation of success. A clear association between oxidative stress and hemodialysis is taught by Sela. Dell'Aglio teaches the administration of cysteine to treat oxidative stress. According to Yamamoto, diabetic nephrology commonly advances to renal failure, which requires hemodialysis. Cysteine in amounts of 10 - 5000 mg is effective in the treatment of nephropathy.

Although Sela et al confirms what is acknowledged in te application, namely that patients undergoing hemodialysis have been observed to be subject to oxidative stress, it teaches a different solution to the problem, namely the use of injection or infusion of heparin..

Dall'Aglio teaches that a combination of tioctic acid and cysteine may be used to treat

conditions caused by oxidative stresses and alterations of mitochondrial energetic metabolism. Diabetes (of no particular type) is mentioned as one of a large number of possible causes of oxidative stress. The experimental data point to the need to use a combination of cysteine and tioctic acid to achieve the desired relief of oxidative stress. importance of both components being set out, for example in the conclusions set out on page 31. As amended claim 10 excludes the possibility of the claim being construed to cover such a synergistic mixture.

The examiner seems to be trying to use the Yamamoto reference in two different ways: one in combination with the other references to suggest use of cysteine to treat oxidative stress and the other as the basis for arguing that patients with nephtopathy take cysteine for other reasons but they would be expected to undergo hemodialysis and so would experience the benefit of the present invention, albeit unwittingly.

Yamamoto describes the use of cysteine to treat diabetic complications. It contemplates effecting this by a daily dose of from 10 - 5000 mg (see column 3 lines 3 - 4 and column 4 lines 29 - 34.. That is to say by continuous treatment with cysteine to effect a long term chronic complications of diabetes, not a specific dose administrations at specific times associated with a particular event, namely hemodialysis at a particular time to treat an acute condition brought about by that treatment. Furthermore, as noted previously, but not commented on by the examiner, Yamamoto talks generally about use of cysteine to treat diabetic complications, but the only definite information given is with respect to cataracts and that in rats treated with cysteine, serum chemical parameters were close to normal in male SD rats in which diabetes had been induced by streptozotocin injection. As pointed out previously streptozotocin induces diabetes by destruction of pancreatic cells thereby preventing insulin production. This is therefore an insulin-dependent form of diabetes (Type 1). The types of condition referred to in the present claims are typically those resulting from non-insulin dependent diabetes.(Type 2) Insulin dependent diabetes is normally treated by insulin injections rather than by hemodialysis.

So far as the examiner's apparent first use of Yamaoto in combination with the other references is concerned, the most that this can be concluded to teach is that nephrology can result in the need for hemodialysis. Hemodialysis can cause oxidative stress. Oxidative stress can be treated with heparin or a combination of cysteine and tioctic acid This is not the present invention.

So far as the alternative application of Yamamoto is concerned, Yamamoto teaches that cysteine can be used to treat diabetes by long term administration of regular doses of cysteine. The examiner implies that such patients will be subject to hemodialysis. This is, however, not inevitable and one can only rely on implicit teaching if the implied steps are in fact inevitable. **Continental Can Co. v. Monsanto Co.** 948 F.2d 1264 20 USPQ2d 1746 (Fed. Cir. 1991). Even if one could assume hemodialyisis for treatment of patients with diabetes this would still not mean that such patients would inevitably be treated in accordance with the claims of the present application. Hemodialysis is typically carried out a few times per week, but not daily .

The art does not teach or in anyway suggest that specific problems that arise when patients are subject to hemodialysysis may be treated or inhibited by use of cysteine as such.. The present claims are limited to this and are therefore novel and non-obvious over this art. In particular claim 10 is specifically directed to a method in which the relationship of the treatment with cysteine or cystine with the dialysis is specifically set out. Nothing in the art points to administering a single dose of cysteine before or after hemodialysis to combat the oxidative stress caused by that dialysis.

It is therefore submitted that the requirements of 35 USC 103 have been complied with and that this application should be allowed.

Respectfully submitted,

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